REMARKS

At the outset, applicants would like to thank Examiner Chernyshev and Primary Examiner Ulm for their time and consideration of the present application at the interview of October 21, 2003. At the interview, the contentions of the outstanding Official Action were discussed.

Applicants believe that the present application has been amended in a manner that places it in condition for allowance at the time of the next Official Action.

Claims 24, 27, 32-33, and 39-43 are pending in the present application. Claims 8-15, 25, 26, 28-31, and 34-38 have been canceled without prejudice and may be the subject of a divisional application. Claims 24, 27, and 32-33 have been amended to more particularly point out and distinctly claim the present invention. New claims 39-43 have been added to vary the scope of the claimed invention. Support for new claims 39-43 may be found in the original claims and in the present specification at page 5, lines 28-30; page 6, lines 1-6; and page 6, lines 6-15.

In the outstanding Official Action, claims 24, 27, and 28 were rejected for reciting the term "non-wildtype". Claims 24 and 27 have been amended to recite "non-wild type". As noted above, claim 28 has been canceled. Support for the term "non-wild type" may be found in the present specification beginning on

page 1. Moreover, applicants note that the original claims also recite this term. Thus, it is believed that claims 24 and 27 have been amended to satisfy the objections of the Official Action.

Claim 26 was rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. It is believed that this rejection has been obviated by the present amendment.

In imposing the rejection, the Official Action alleged that the present specification did not support the recitation to an "active fragment" of an Aβ peptide.

As noted above, claim 26 has been canceled. Moreover, applicants note that none of the claims recite an "active fragment" of Aβ peptide. Thus, applicants believe that claims 24, 27, 32-33 and 39-43 are supported by the present disclosure.

In the outstanding Official Action, claims 24-38 were rejected under 35 USC 112, second paragraph, as allegedly being indefinite. This rejection is respectfully traversed.

The outstanding Official Action rejected the claims for reciting the terms "non-wildtype", "protofibril", and "fibril". As noted above, the claims have been amended to recite a "non-wild type" protofibril. This term is found in the specification and claims and is believed to be understood by one of ordinary skill in the art. Moreover, applicants believe that one of

ordinary skill in the art would also find the terms "protofibril" and "fibril" definite. Indeed, the Examiner's attention is directed to the WALSH et al. article which clearly utilizes this terminology. Thus, it is believed that the claimed invention is definite to one of ordinary skill in the art.

In the Official Action, claims 24-38 were rejected under 35 USC 102(b) as allegedly being anticipated by SCHENK et al. This rejection is respectfully traversed.

Applicants believe that SCHENK et al. fail to disclose or suggest the claimed invention. As noted at the interview, applicants believe that SCHENK et al. fail to disclose or suggest the arctic mutation of the claimed invention.

Indeed, as suggested at the interview by Examiner Chernyshev and Primary Examiner Ulm, amended claim 24 recites a method for the prevention or treatment of Alzheimer's disease in a subject having or suspected of having Alzheimer's disease, comprising administering to the subject a therapeutically effective amount of a non-wild type protofibril, wherein the non-wild type protofibril comprises SEQ ID NO:1. Applicants appreciate the suggestion set forth at the interview and believe that claim 24 is allowable.

The Examiner's attention is also directed to new claims 39-43. Independent claim 39 is directed to a method for the prevention or treatment of Alzheimer's disease. The protofibril

of claim 39 comprises the peptide selected from the group consisting of Aβ39-Arc (Amino Acids 1-39 of SEQ ID NO:1), Aβ40-Arc (Amino Acids 1-40 of SEQ ID NO:1) and Aβ42-Arc (SEQ ID NO:1). As noted above, SCHENK et al. fail to disclose or suggest the arctic mutation. As a result, it is believed that claim 39 is also allowable. Applicants note that claim 40 is dependent on claim 39.

As to independent claim 41, claim 41 recites a method for the prevention or treatment of Alzheimer's disease in a subject having or suspected of having Alzheimer's disease, administering to the subject a therapeutically effective amount of a non-wild type protofibril, wherein the protofibril comprises a mutated Aβ peptide comprising the mutation $Glu_{22} \rightarrow Gly_{22}$. Claim 42 is dependent on claim 41. Applicants believe that claims 41 and 42 are allowable for the reasons noted above. SCHENK et al. do not teach or suggest the arctic mutation.

Claims 27 and 32 are directed to a method for prevention and treatment of Alzheimer's disease, wherein a therapeutically effective antibody is administered to the subject. At this time, applicants would like to clarify the Interview Summary of October 21, 2003. While the Interview Summary recommends limiting the claims to the use of antibodies that bind protofibrils of Arc Aβ to the exclusion of wild type Aβ, applicants note that the present invention is actually

directed to antibodies which have properties that are identical to antibodies raised against Aβ-Arc peptides in a protofibril confirmation. While SCHENK et al. may teach a method of treating Alzheimer's patients with the administration of an antibody to an Aβ peptide, SCHENK et al. fail to disclose or suggest antibodies raised against an Aβ-Arc peptide in a protofibril confirmation. Indeed, SCHENK et al. teach that the antibodies specifically bind at Aβ peptide (see SCHENK et al., page 17, lines 35-39).

Thus, in view of the above, it is believed that SCHENK et al. fail to anticipate or render obvious claims 24, 27, 32, 33, and 39-43.

At this time, applicants would also like to present the article by FORSELL et al. At the interview, Examiner Chernyshev and Primary Examiner Ulm asked that this article be submitted. The article is directed to an amyloid precursor protein mutation at codon 713 (Ala → Val). Thus, the article does not pertain to the arctic mutation of the present invention. Applicants also note that this reference was provided with the Information Disclosure Statement submitted on March 12, 2002 and has already been considered by the Patent Office.

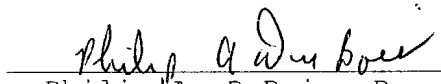
In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 24, 27, 32-33, and 39-43,

as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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**APPENDIX:**

The Appendix includes the following item(s):

- WALSH et al. "Amyloid β-Protein Fibrillogenesis"

- FORSELL et al. "Amyloid precursor protein mutation at codon 713 (Ala → Val) does not cause schizophrenia: non-pathogenic variant found at codon 705 (silent)"